

*Subj 4  
cont'd*

provided that when X and Y are oxygen atoms and \_\_\_\_\_ is a single bond, R<sup>4</sup> is not an acyl, or a salt thereof.

26. (NEW) A method of claim 25, which is a method for suppressing β-amyloid toxicity.

27. (NEW) A method of claim 25, which is a method for preventing and/or treating neurodegenerative diseases.

*Subj 5*

28. (NEW) A method of claim 22, which is a method for suppressing β-amyloid toxicity.

29. (NEW) A method of claim 22, which is a method for preventing and/or treating neurodegenerative diseases.

## REMARKS

### I. Claim Amendments

Claims 4 and 16 – 21 have been cancelled without prejudice to the filing of future continuing applications.

Newly added claims 25-29 encompass the subject matter of cancelled claims 16-21.

Claims 1, 2, 3, 10, 11, 12 and 22 have been amended to conform the claims to the invention of the elected species in response to the Examiner's request for restriction of the claims. Applicants reserve the right to file future continuing applications directed to the non-elected species of the invention as filed.

Claim 15 has been amended to more clearly recite the inclusion of a carrier, excipient or diluent component of the claimed pharmaceutical composition. Support for this amendment can be found in the specification and claims as filed, as for example on page 64 line 26 to page 67 line 9 of the specification.

Claim 22 has been amended to more clearly point out the specific elements of the claimed invention, and to better identify the specific substituents referred to therein.

No amendment of inventorship is necessitated by these amendments.

## **II. Rejection based upon an improper Markush group.**

Applicants have amended the pending claims to conform to the elected species as designated in response to the Examiner's restriction requirement.

The claims do not recite an improper Markush group. Early allowance of the claims is respectfully solicited.

## **III. Rejections under 35 U.S.C. 112, second paragraph.**

Claims 19-21 have been cancelled, without prejudice, and the subject matter encompassed in newly added claims 28 – 29. The newly added claims are free from the Examiner's objection to the term "agent".

## **IV. Claims 16-18 rejected as substantially duplicative of claim 15.**

Claims 16-18 have been cancelled without prejudice, and the subject matter of the claims encompassed within the newly added claims 25-27. The newly added claims are patentably distinct over claim 15.

## **V. Rejection under 35 USC §102(b).**

Claims 1-12 and 14 have been rejected as anticipated by the teaching of certain asserted references. Applicants have amended the claims to conform to the elected species of invention in response to the Examiner's restriction requirement.

The Claims as amended are free from the asserted art. None of the asserted references teach each an every limitation of the claimed invention, and thus fail to anticipate the claimed invention. This is clearly illustrated in the attached Appendix A. In Appendix A, applicants provide a summary table which compares the structure of the claimed invention with that of the cited art references. Also provided by Appendix A is a listing of the chemical structures taught by the asserted art, and the components of the structures compared with that of the claimed invention.

Each rejection is traversed below with reference to Appendix A.

1) Claims 1-12 and 14 have been rejected in view of the teaching of Reference A. Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

2) Claims 1-12 and 14 had been rejected in view of the teaching of Reference U.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

3) Claims 1-12 and 14 had been rejected in view of the teaching of Reference N.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

4) Claims 1-12 and 14 had been rejected in view of the teaching of Reference B.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

5) Claims 1-12 and 14 had been rejected in view of the teaching of Reference O.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach the combination of both of the claimed limitations, this rejection must be withdrawn.

6) Claims 1-12 and 14 had been rejected in view of the teaching of Reference P.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

7) Claims 1-12 and 14 had been rejected in view of the teaching of Reference C.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

8) Claims 1-12 and 14 had been rejected in view of the teaching of Reference Q.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

9) Claims 1-12 and 14 had been rejected in view of the teaching of Reference R.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

10) Claims 1-12 and 14 had been rejected in view of the teaching of Reference S.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

11) Claims 1-12 and 14 had been rejected in view of the teaching of Reference T.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

12) Claims 1-12 and 14 had been rejected in view of the teaching of Reference N1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

13) Claims 1-12 and 14 had been rejected in view of the teaching of Reference O1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

14) Claims 1-12 and 14 had been rejected in view of the teaching of Reference P1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

15) Claims 1-12 and 14 had been rejected in view of the teaching of Reference

Q1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

16) Claims 1-12 and 14 had been rejected in view of the teaching of Reference

R1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

17) Claims 1-12 and 14 had been rejected in view of the teaching of Reference

S1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

18) Claims 1-12 and 14 had been rejected in view of the teaching of Reference T1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

19) Claims 1-12 and 14 had been rejected in view of the teaching of Reference N2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

20) Claims 1-12 and 14 had been rejected in view of the teaching of Reference O2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

21) Claims 1-12 and 14 had been rejected in view of the teaching of Reference P2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

22) Claims 1-12 and 14 had been rejected in view of the teaching of Reference Q2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

23) Claims 1-12 and 14 had been rejected in view of the teaching of Reference R2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

24) Claims 1-12 and 14 had been rejected in view of the teaching of Reference S2.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

25) Claims 1-12 and 14 had been rejected in view of the teaching of Reference T2 WO 9620925.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

26) Claims 1-12 and 14 had been rejected in view of the teaching of Reference N3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

27) Claims 1-12 and 14 had been rejected in view of the teaching of Reference O3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

28) Claims 1-12 and 14 had been rejected in view of the teaching of Reference P3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

29) Claims 1-12 and 14 had been rejected in view of the teaching of Reference Q3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

30) Claims 1-12 and 14 had been rejected in view of the teaching of Reference R3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

31) Claims 1-12 and 14 had been rejected in view of the teaching of Reference S3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

32) Claims 1-12 and 14 had been rejected in view of the teaching of Reference T3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

33) Claims 1-12 and 14 had been rejected in view of the teaching of Reference N4.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

34) Claims 1-12 and 14 had been rejected in view of the teaching of Reference O4.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

35) Claims 1-12 and 14 had been rejected in view of the teaching of Reference P4.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

36) Claims 1-12 and 14 had been rejected in view of the teaching of Reference Q4.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

37) Claims 1-12 and 14 had been rejected in view of the teaching of Reference V.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

38) Claims 1-12 and 14 had been rejected in view of the teaching of Reference W.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

39) Claims 1-12 and 14 had been rejected in view of the teaching of Reference X.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

40) Claims 1-12 and 14 had been rejected in view of the teaching of Reference U1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

41) Claims 1-12 and 14 had been rejected in view of the teaching of Reference V1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

42) Claims 1-12 and 14 had been rejected in view of the teaching of Reference W1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

43) Claims 1-12 and 14 had been rejected in view of the teaching of Reference X1.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

44) Claims 1-12 and 14 had been rejected in view of the teaching of Reference U2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

45) Claims 1-12 and 14 had been rejected in view of the teaching of Reference V2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

46) Claims 1-12 and 14 had been rejected in view of the teaching of Reference W2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

47) Claims 1-12 and 14 had been rejected in view of the teaching of Reference X2.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach the combination of both of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

48) Claims 1-12 and 14 had been rejected in view of the teaching of Reference U3.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

49) Claims 1-12 and 14 had been rejected in view of the teaching of Reference V3.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

50) Claims 1-12 and 14 had been rejected in view of the teaching of Reference W3.

Claim 1 as now amended recites the limitation that:

$R^1$  and  $R^2$  each represents an aliphatic hydrocarbon group or

$R^1$  and  $R^2$  form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic ring which may be substituted, and

$R^3$  represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

51) Claims 1-12 and 14 had been rejected in view of the teaching of Reference X3.

Claim 1 as now amended recites the limitation that:

R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or

R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbocyclic or heterocyclic ring which may be substituted, and

R<sup>3</sup> represents an aromatic group which may be substituted.

The cited reference fails to teach either of these limitations.

As the asserted art does not teach all of the claimed limitations, this rejection must be withdrawn.

#### V. Examiner's Comments

- 1) Applicants acknowledge the Examiner's finding that references noted as X on the IPER are not, in fact, X references.
- 2) Applicants have previously submitted copies of all cited references to the USPTO. Given the possibility that certain copies did not reach the Examiner, copies of the references crossed out by the Examiner are herewith supplied once again, along with a copy of the original Form PTO-1449 for the Examiner's use. References already considered are not being resubmitted.
- 3) Applicants thank the Examiner for pointing out the allowable subject matter of claims 24 and 13.

## **VI. Conclusion**

Reconsideration of the claims as amended, in view of the traverse made above, and early allowance of the claims is requested.

Should the Examiner believe that a conference with applicants' attorney would advance prosecution of this application, he is respectfully requested to call applicants' attorney at (847) 383-3372.

Respectfully submitted,



Dated: February 2, 2001

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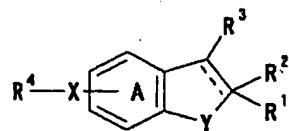
Philippe Y. Riesen, Reg. No. 35,657  
Mark Chao, Ph.D., Reg. No. 37,293  
Attorney for Applicants  
Customer No. 23115

Application No.: 09/445193  
Filed: December 2, 1999  
1<sup>st</sup> Inventor: OHKAWA et al.  
For: Heterocyclic Compounds, Production and Use  
Atty. Dkt. No. 2470 US0P

Art Unit: 1625  
Examiner: B. Robinson  
Allowed:  
Batch:  
Paper No.:

**APPENDIX A to Response and Amendment "A" filed herewith.**

**Table: pages i and ii  
Structures: pages 1-12**



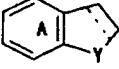
○ : same as reference

- : difference

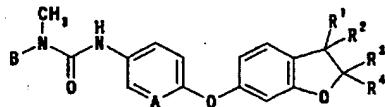
restriction ① : R<sup>1</sup> and R<sup>2</sup> each represents an aliphatic hydrocarbon group or R<sup>1</sup> and R<sup>2</sup> form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic ring which may be substituted;

restriction ② : R<sup>3</sup> represents an aromatic group which may be substituted;

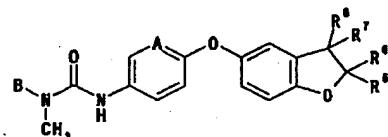
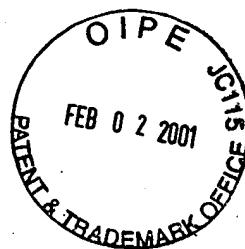
ref.		R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	X	①	②	①+②
A	○	○	○	○	○	○	○	-	-
U	○	○	○	○	○	○	-	-	-
N	○	○	○	○	○	○	-	-	-
B	○	○	○	○	○	○	○	-	-
O	○	○	○	○	○	○	○	-	-
P	○	○	○	○	○	○	-	-	-
C	○	○	○	○	○	○	○	-	-
Q	○	○	○	○	○	○	-	-	-
R	○	○	○	○	○	○	○	-	-
S	○	○	○	○	○	○	○	-	-
T	○	○	○	○	○	○	○	-	-
N1	○	○	○	○	○	○	○	-	-
O1	○	○	○	○	○	○	○	-	-
P1	○	○	○	○	○	○	○	-	-
Q1	○	○	○	○	○	○	○	-	-
R1	○	○	○	○	-	○	-	-	-
S1	○	○	○	○	○	○	○	-	-
T1	○	○	○	○	○	○	-	○	-
N2	○	○	○	○	○	○	○	-	-
O2	○	○	○	○	○	○	-	-	-
P2	○	○	○	○	○	○	-	-	-

ref.		R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	X	①	②	①+②
Q2	○	○	○	○	○	○	-	-	-
R2	○	○	○	○	○	○	○	-	-
S2	○	○	○	○	○	○	○	-	-
T2	○	○	○	○	○	○	○	-	-
N3	○	○	○	○	○	○	-	-	-
O3	○	○	○	○	○	○	○	-	-
P3	○	○	○	○	○	○	○	-	-
Q3	○	○	○	○	○	○	○	-	-
R3	○	○	○	○	○	○	○	-	-
S3	○	○	○	○	○	○	-	-	-
T3	○	○	○	○	○	○	-	-	-
N4	○	○	○	○	○	○	-	-	-
O4	○	○	○	○	○	○	-	○	-
P4	○	○	○	○	○	○	○	-	-
Q4	○	○	○	○	-	○	-	-	-
V	○	○	○	○	○	○	○	-	-
W	○	○	○	○	○	○	○	-	-
X	○	○	○	○	○	○	-	-	-
U1	○	○	○	○	○	○	○	-	-
V1	○	○	○	○	○	○	-	-	-
W1	○	○	○	○	○	○	-	-	-
X1	○	○	○	○	○	○	○	-	-
U2	○	○	○	○	○	○	-	○	-
V2	○	○	○	○	○	○	-	-	-
W2	○	○	○	○	○	○	-	-	-
X2	○	○	○	○	○	○	○	-	-
U3	○	○	○	○	○	○	-	-	-
V3	○	○	○	○	○	○	-	-	-
W3	○	○	○	○	○	○	-	-	-
X3	○	○	○	○	○	○	-	-	-

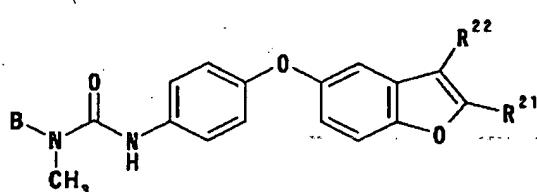
Ref A



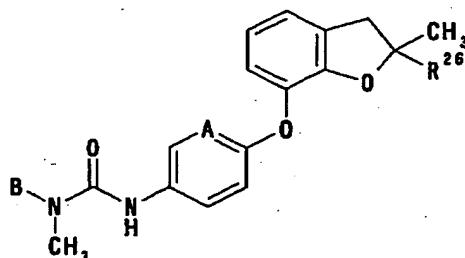
R<sup>1</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, <sup>1</sup>C<sub>3</sub>H<sub>7</sub>; R<sup>2</sup> = H;  
 R<sup>3</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, <sup>1</sup>C<sub>3</sub>H<sub>7</sub>, <sup>5</sup>C<sub>4</sub>H<sub>9</sub>;  
 R<sup>4</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>; A = CH, N,  
 C-Cl, C-NO<sub>2</sub>, C-CF<sub>3</sub>; B = H, CH<sub>3</sub>, OCH<sub>3</sub>



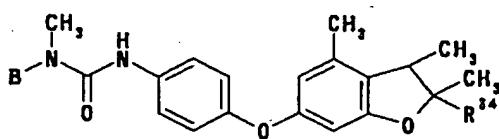
R<sup>5</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, <sup>1</sup>C<sub>4</sub>H<sub>9</sub>, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>,  
 O<sup>1</sup>C<sub>3</sub>H<sub>7</sub>; R<sup>6</sup> = H, CH<sub>3</sub>; R<sup>7</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>,  
<sup>1</sup>C<sub>3</sub>H<sub>7</sub>, <sup>5</sup>C<sub>4</sub>H<sub>9</sub>; R<sup>8</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>; A = CH,  
 N, C-Cl; B = H, CH<sub>3</sub>, OCH<sub>3</sub>



R<sup>21</sup> = H, <sup>1</sup>C<sub>3</sub>H<sub>7</sub>, <sup>5</sup>C<sub>4</sub>H<sub>9</sub>; R<sup>22</sup> = H, C<sub>2</sub>H<sub>5</sub>,  
<sup>1</sup>C<sub>3</sub>H<sub>7</sub>; B = H, CH<sub>3</sub>, OCH<sub>3</sub>

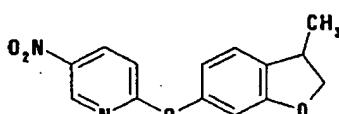


R<sup>26</sup> = H, CH<sub>3</sub>; A = CH, N;  
 B = H, CH<sub>3</sub>, OCH<sub>3</sub>

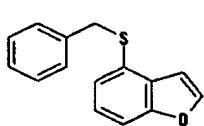


R<sup>34</sup> = CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>; B = H, CH<sub>3</sub>, OCH<sub>3</sub>

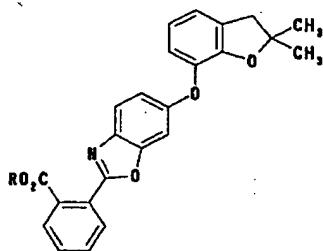
Ref. U



Ref. N

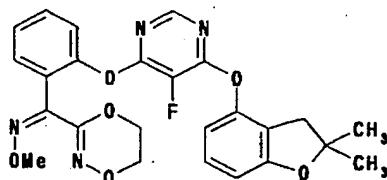


Ref. B

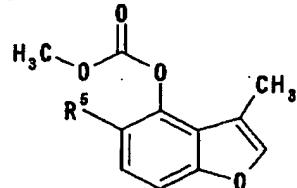


R = H, Me

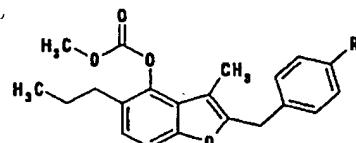
Ref. O



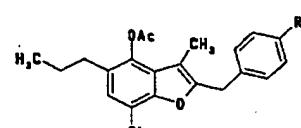
**Ref. P**



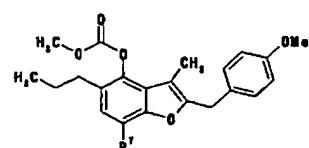
$R^5 = H, (CH_2)_2CH_3$



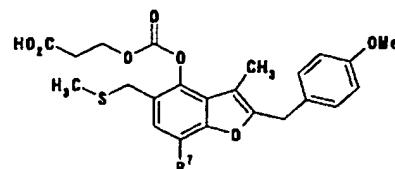
$R = H, OCH_3$



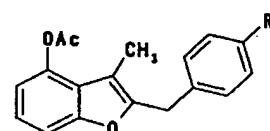
$R = OAc, OCH_3$



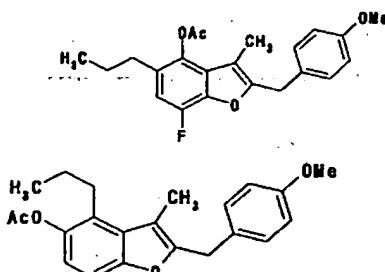
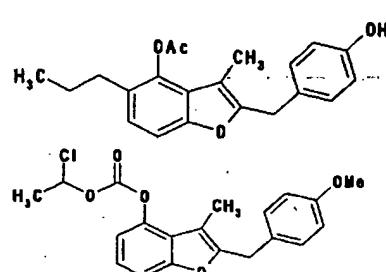
$R^7 = F, Cl$



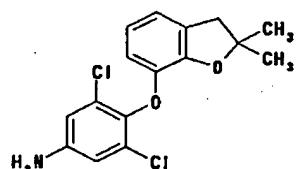
$R^7 = F, (CH_2)_2CH_3$



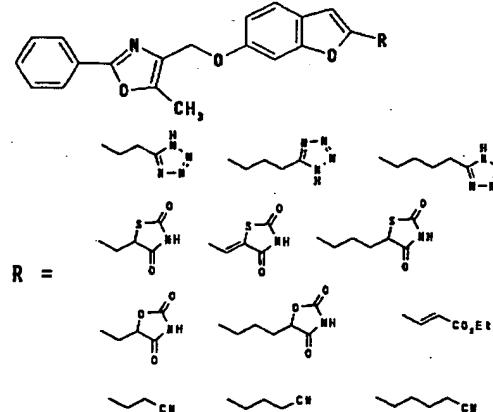
$R = H, OCH_3$



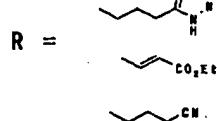
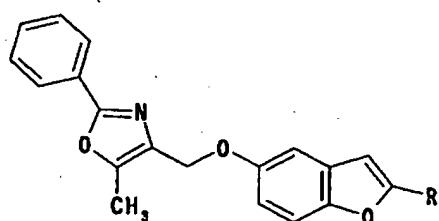
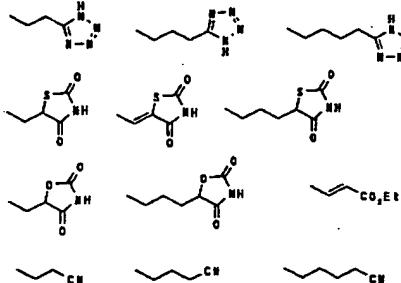
**Ref. C**



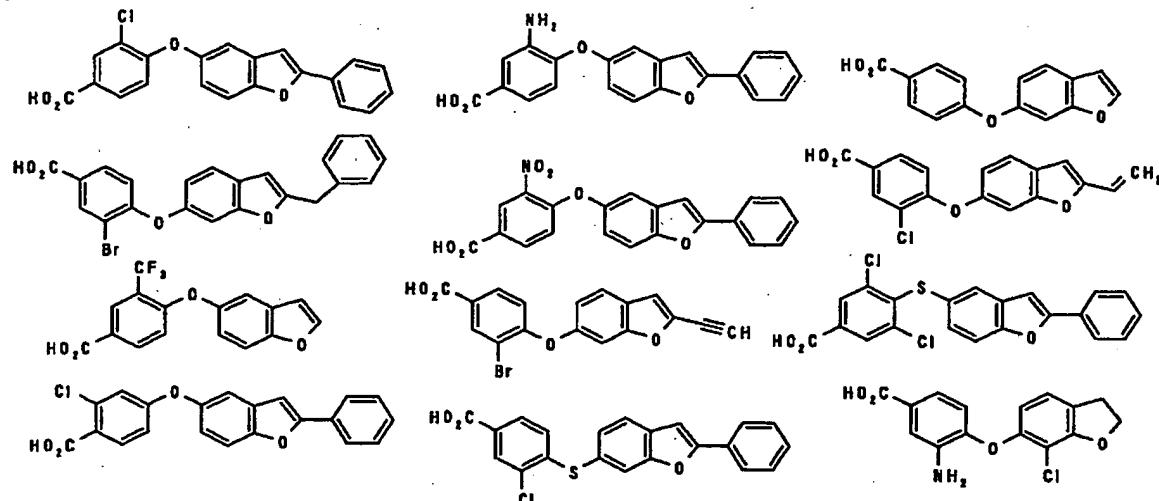
**Ref. Q**



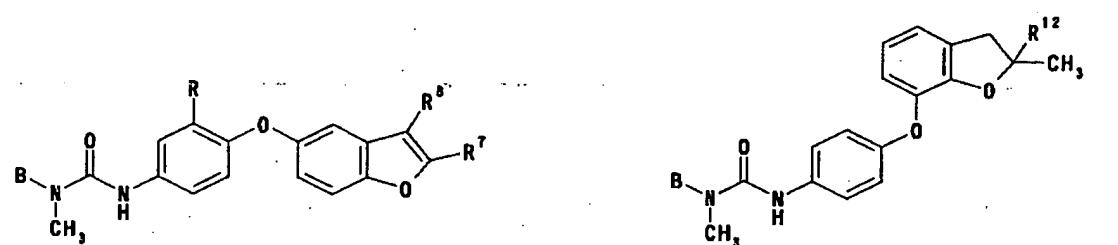
$R =$



Ref. R, S

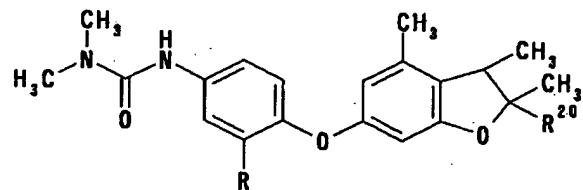


Ref. T



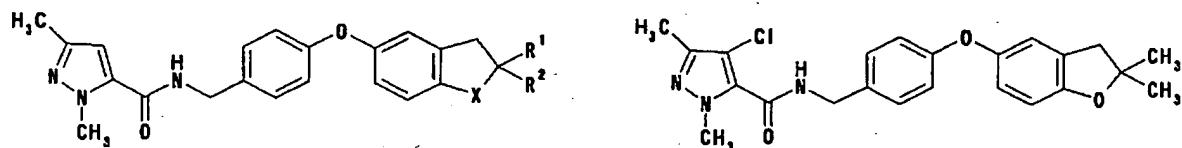
$R^7 = H, {}^1C_3H_7, {}^1C_4H_9; R^8 = H, C_2H_5, {}^nC_3H_7,$   
 ${}^1C_3H_7; R = H, NO_2, Cl, CF_3; B = H,$   
 $CH_3, OCH_3$

$R^{12} = H, CH_3, A = CH, N,$   
 $C-NO_2, B = CH_3, OCH_3$

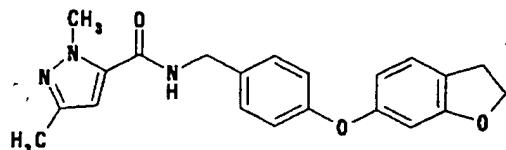


$R^{20} = CH_3, C_2H_5; R = H, CF_3$

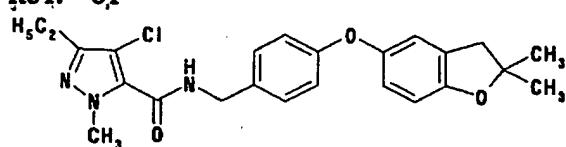
Ref. N1



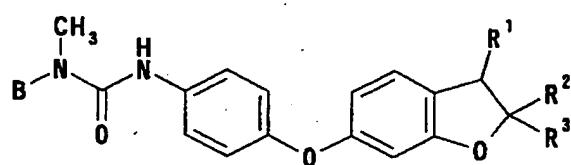
$X = O, S; R^1 = H, CH_3; R^2 = H, CH_3$



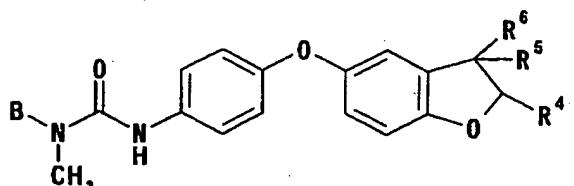
Ref. O1



Ref. P1

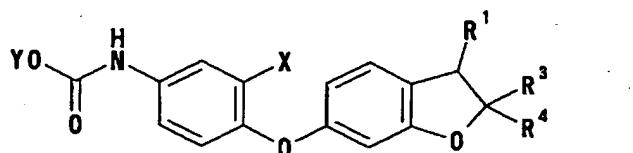


$R^1 = H, CH_3, C_2H_5; R^2 = H, CH_3, C_2H_5;$   
 $R^3 = H, CH_3, C_2H_5; B = CH_3, OCH_3$

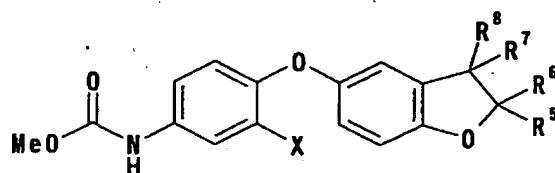


$R^4 = H, CH_3, OCH_3, OC_2H_5; R^5 = H, CH_3,$   
 $C_2H_5; R^6 = H, CH_3, C_2H_5; B = CH_3, OCH_3$

Ref. Q1

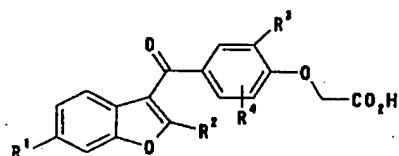


$R^1 = H, CH_3; R^3 = H, CH_3; R^4 = H, CH_3, C_2H_5;$   
 $X = H, Cl; Y = CH_3, C_2H_5, ^1C_3H_7$



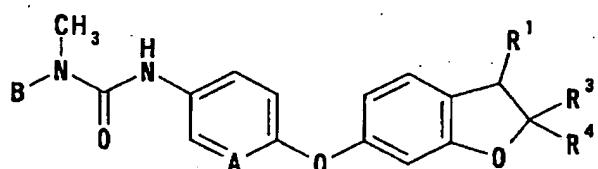
$R^5 = CH_3, OCH_3; R^6 = H, CH_3; R^7 = H, CH_3,$   
 $C_2H_5; R^8 = H, CH_3; X = H, Cl$

Ref. R1

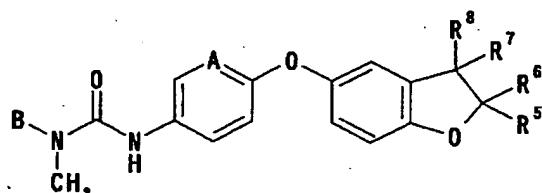


$R^1$  is lower alkyl, lower alkoxy, halogen, etc;  $R^2$  is lower alkyl;  $R^3$  and  $R^4$  are H, lower alkyl. The compounds of this reference are different from those of Claim 1.

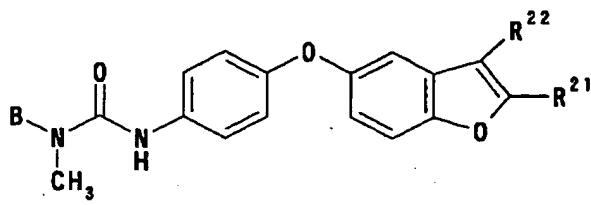
Ref. S1



$R^1 = H, CH_3, C_2H_5, ^1C_3H_7; R^3 = CH_3, C_2H_5,$   
 $^1C_3H_7, ^2C_4H_9; R^4 = H, CH_3, C_2H_5; A = CH_3,$   
 $N, C-Cl, C-NO_2, C-CF_3; B = H, CH_3, OCH_3$

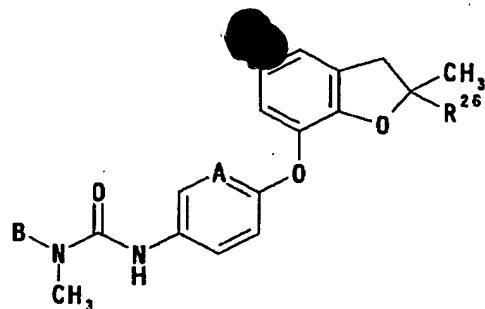


$R^5 = H, CH_3, ^1C_4H_9, OCH_3, OC_2H_5; R^6 =$   
 $H, CH_3; R^7 = H, CH_3, C_2H_5, ^1C_3H_7, ^2C_3H_7;$   
 $R^8 = H, CH_3, C_2H_5; A = CH_3, N, C-Cl;$   
 $B = H, CH_3, OCH_3$

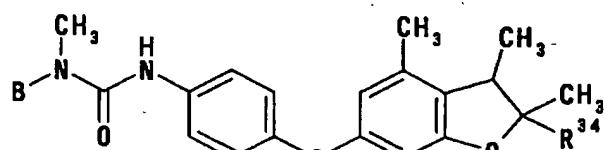


$R^{21} = H, ^1C_3H_7, ^1C_4H_9; R^{22} = H, C_2H_5, ^1C_3H_7;$

$B = H, CH_3, OCH_3$

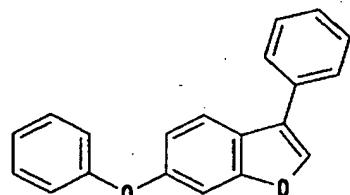


$R^{26} = H, CH_3; A = CH, N; B = H, CH_3, OCH_3$

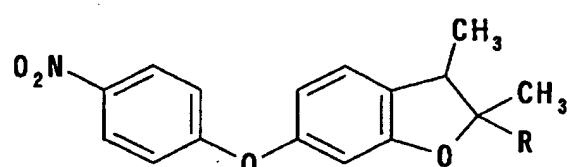


$R^{34} = CH_3, C_2H_5; B = H, CH_3, OCH_3$

Ref. T1

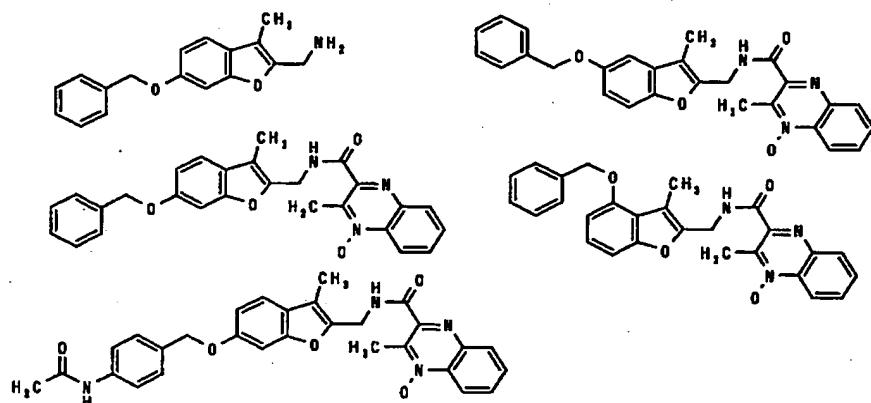


Ref. N2

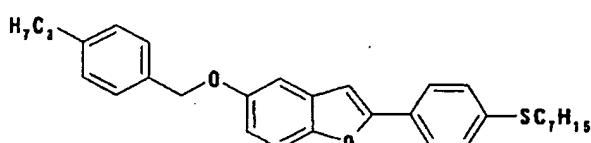


$R = CH_3, C_2H_5, OCH_3$

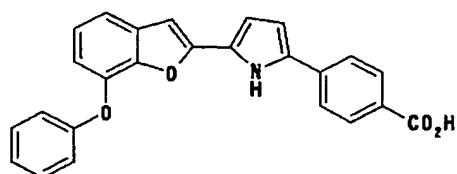
Ref. 02



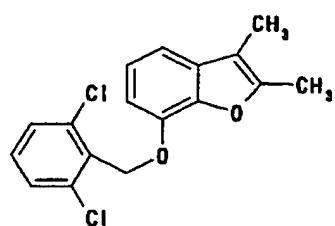
Ref. P2



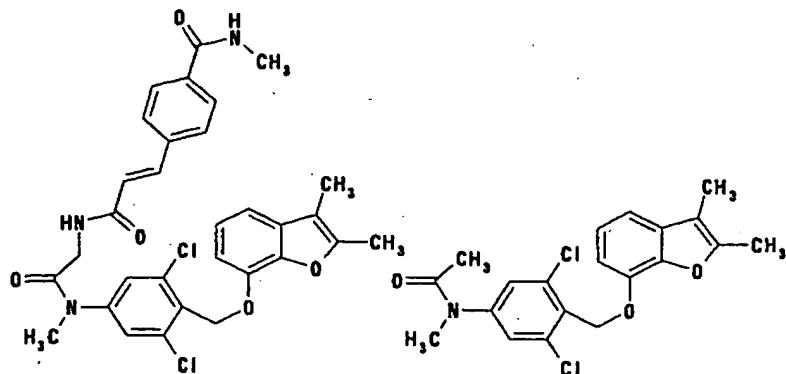
Ref. Q2



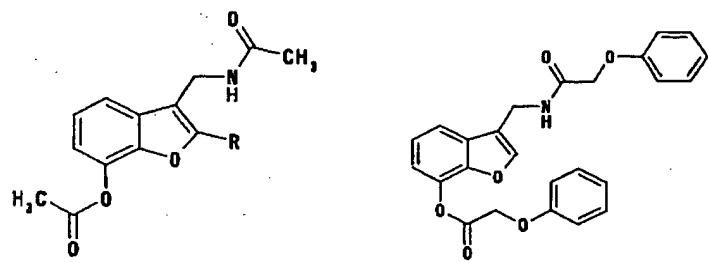
Ref. R2



Ref. S2

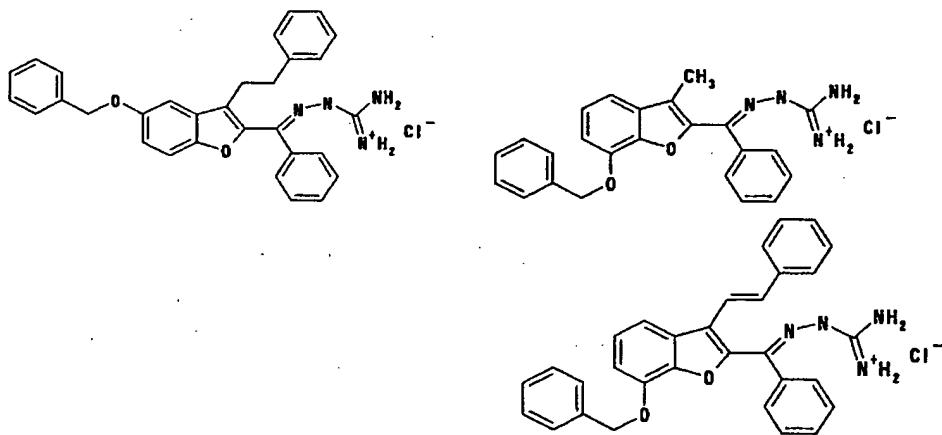


Ref. T2

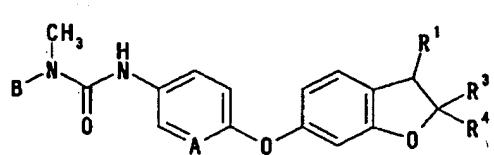


R = H, CH<sub>3</sub>

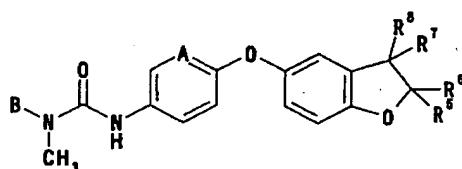
Ref. N3



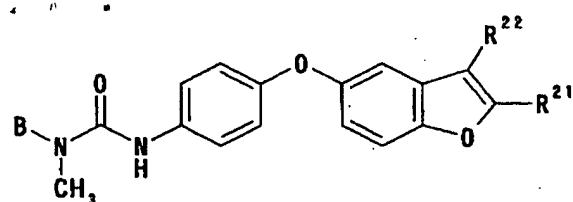
Ref. O3



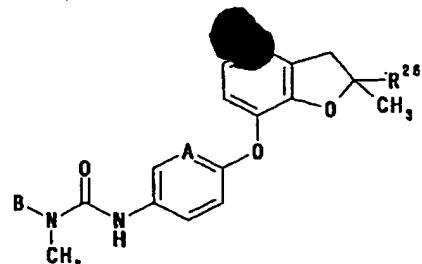
R<sup>1</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, <sup>1</sup>C<sub>3</sub>H<sub>7</sub>; R<sup>3</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>;  
 R<sup>4</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>; A = CH, N, C-Cl, C-NO<sub>2</sub>, C-CF<sub>3</sub>; B = H, CH<sub>3</sub>, OCH<sub>3</sub>



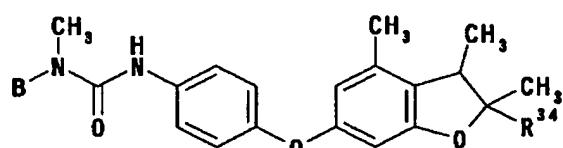
R<sup>5</sup> = H, CH<sub>3</sub>, <sup>1</sup>C<sub>4</sub>H<sub>9</sub>, OCH<sub>3</sub>, OC<sub>2</sub>H<sub>5</sub>, O<sup>1</sup>C<sub>3</sub>H<sub>7</sub>;  
 R<sup>6</sup> = H, CH<sub>3</sub>; R<sup>7</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, <sup>1</sup>C<sub>3</sub>H<sub>7</sub>;  
 R<sup>8</sup> = H, CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>; A = CH, N, C-Cl;  
 B = H, CH<sub>3</sub>, OCH<sub>3</sub>



$R^{21} = H, CH_3, ^1C_3H_7, ^1C_4H_9; R^{22} = H, C_2H_5, ^1C_3H_7,$   
 $^1C_3H_7; B = H, CH_3, OCH_3$

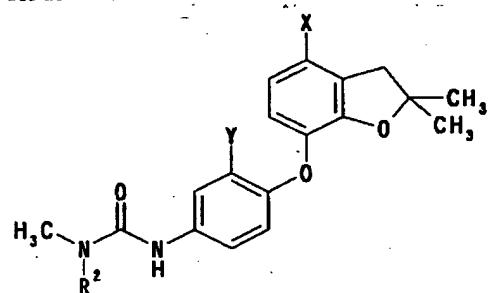


$R^{26} = H, CH_3; A = CH, N;$   
 $B = H, CH_3, OCH_3$

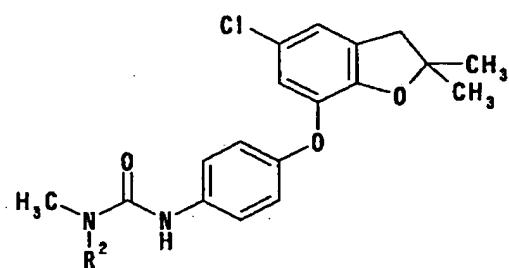


$R^{34} = CH_3, C_2H_5; B = H, CH_3, OCH_3$

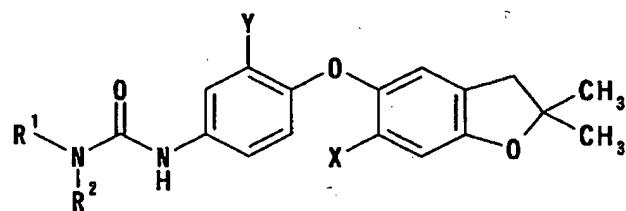
### Ref. P3



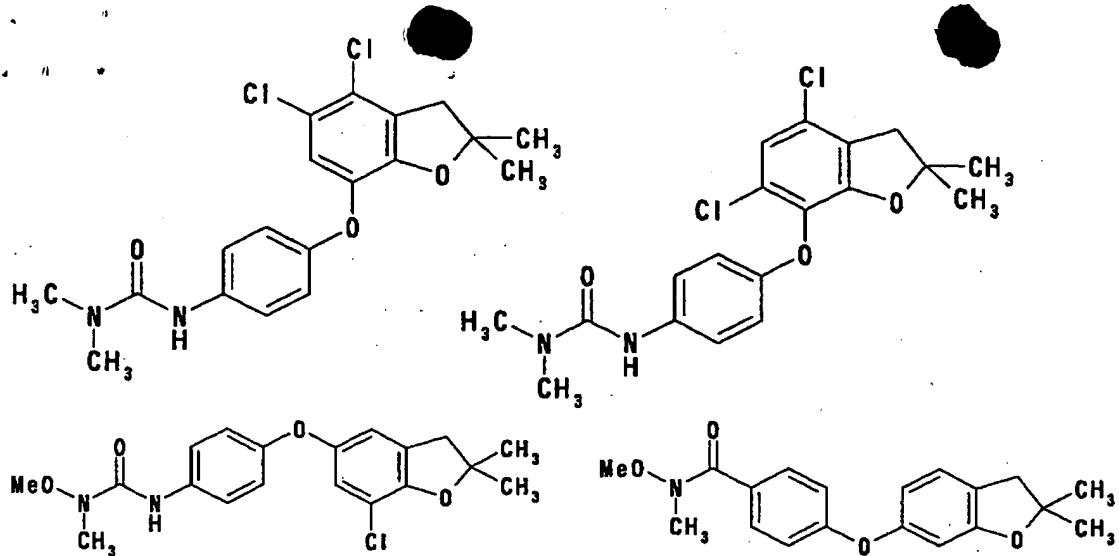
$X = H, F, Cl, Br, CF_3; Y = H,$   
 $F, Cl; R^2 = CH_3, OCH_3$



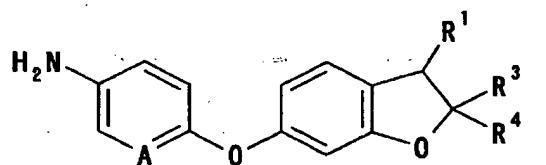
$R^2 = CH_3, OCH_3$



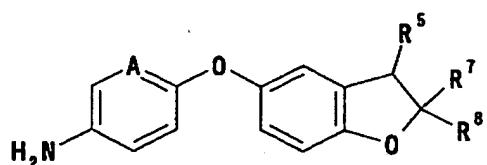
$X = H, Cl, Br; Y = H, F, Cl, CF_3; R^1 = CH_3, C_2H_5;$   
 $R^2 = CH_3, OCH_3, C_2H_5, OC_2H_5, CH_2CH=CH_2, CH_2C\equiv CH$



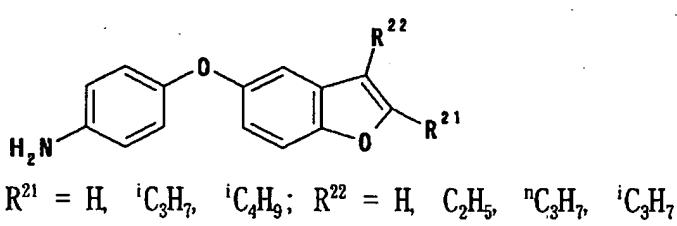
Ref. Q3



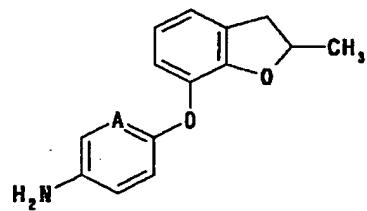
$R^1 = H, CH_3, C_2H_5, ^nC_3H_7; R^3 = H, CH_3, C_2H_5, ^nC_3H_7, ^iC_3H_7, ^sC_4H_9; R^4 = H, CH_3, C_2H_5; A = CH, N, C-Cl, C-NO_2, C-CF_3$



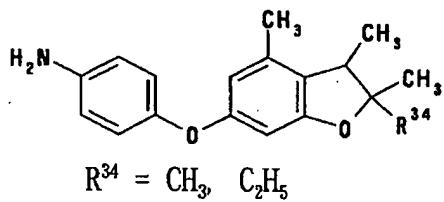
$R^5 = H, CH_3, ^iC_3H_7, OCH_3, OC_2H_5, O^iC_3H_7; R^7 = H, CH_3, C_2H_5, ^nC_3H_7, ^iC_3H_7, R^8 = H, CH_3, C_2H_5; A = CH, N, C-Cl$



$R^{21} = H, ^iC_3H_7, ^iC_4H_9; R^{22} = H, C_2H_5, ^nC_3H_7, ^iC_3H_7$

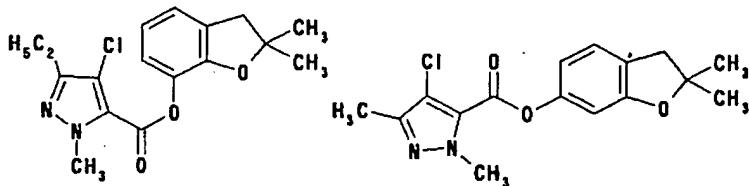


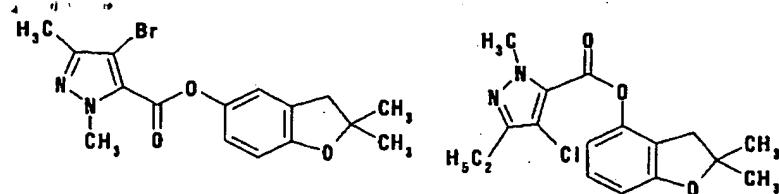
$A = CH, N$



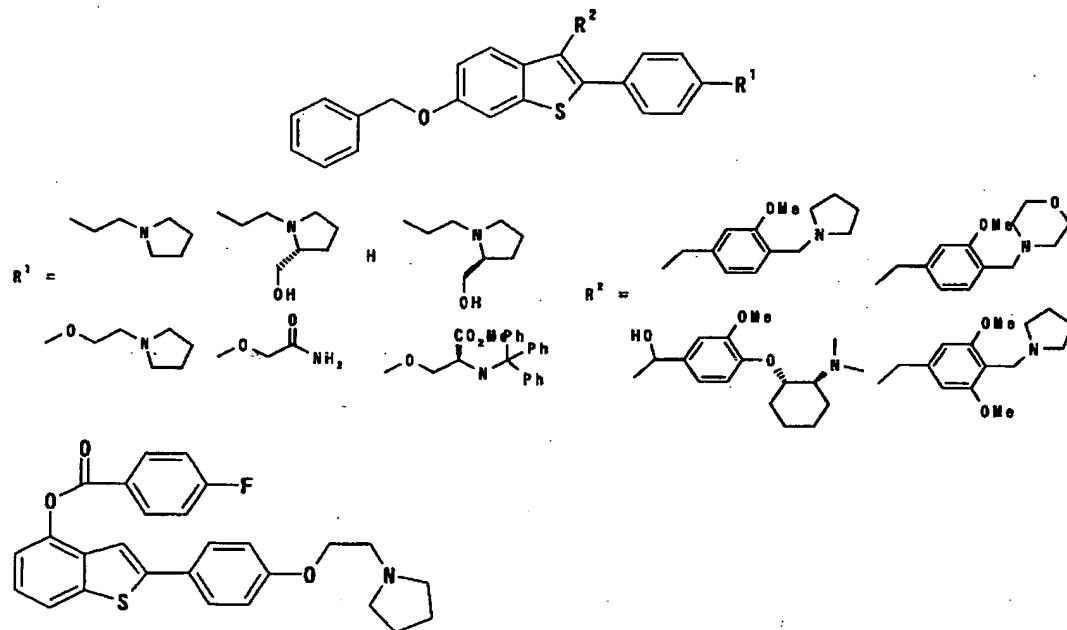
$R^{34} = CH_3, C_2H_5$

Ref. R3

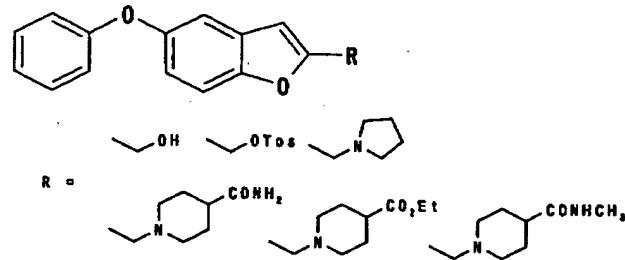




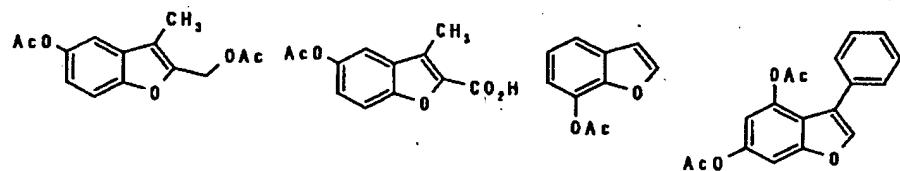
Ref. S3



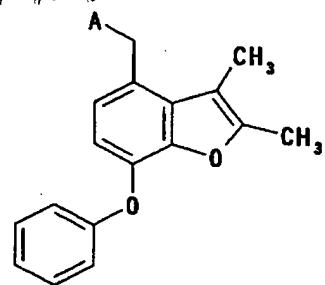
Ref. T3, N4



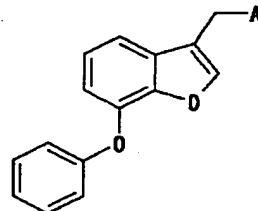
Ref. 04



**Ref. P4**

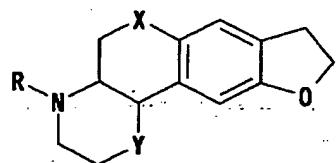


$A = 1-(1, 2, 4\text{-triazolyl}),$   
 $1-(1, 2, 3\text{-triazolyl}),$   
 $1\text{-tetrazolyl}, 2\text{-tetrazolyl}$



$A = 1\text{-imidazolyl},$   
 $1-(1, 2, 4\text{-triazolyl}),$   
 $1\text{-tetrazolyl}, 2\text{-tetrazolyl}$

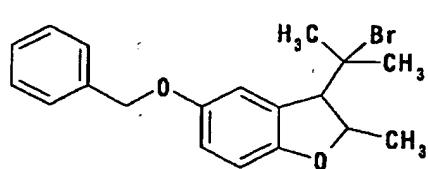
**Ref. Q4**



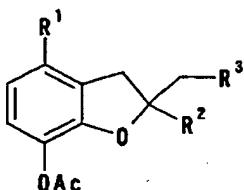
X and Y, which may be the same or different, each represents an oxygen atom or  $\text{CH}_2$ ; R represents a hydrogen atom or a  $C_{1-10}$  alkyl,  $C_{3-10}$  alkenyl radical, each of which may be straight or branched chain and each of which may optionally be substituted by a cycloalkyl radical having from 3 to 8 carbon atoms, or by an aryl radical selected from the radicals phenyl, thienyl and pyridyl, each of which may optionally be substituted by one or more substituents selected from halogen atoms, hydroxy radicals, and alkyl and alkoxy radicals each having 1 to 6 carbon atoms in straight or in branched chain; n represents 0 or 1 when X represents  $\text{CH}_2$  and 1 when X represents an oxygen atom.

The compounds of this reference are different from those of Claim 1.

**Ref. V**

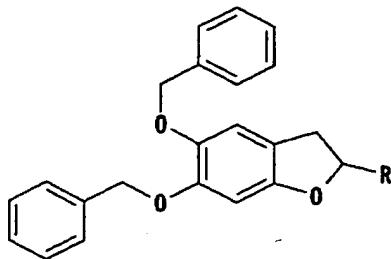


**Ref. W**



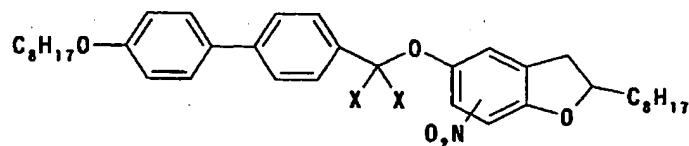
$R^1 = H, Me;$   $R^2 = H, Me;$   $R^3 = H, C_5H_{11}$   
 $R^2, R^3 = -(CH_2)_4-$

Ref. X



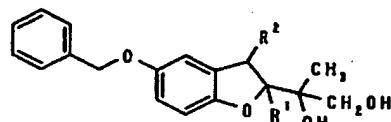
R = CO<sub>2</sub>Et, CH<sub>2</sub>OH, CHO

Ref. U1



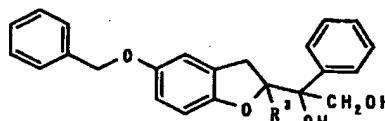
X = H, =O; 6-NO<sub>2</sub>, 7-NO<sub>2</sub>;

Ref. V1



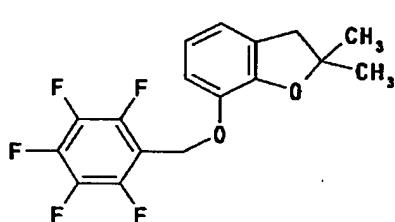
R<sup>1</sup> = H, CH<sub>3</sub>; R<sup>2</sup> = H, CH<sub>3</sub>

Ref. W1

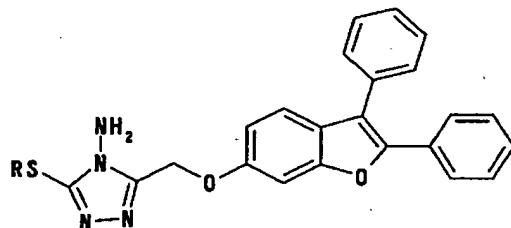


R<sup>3</sup> = H, CH<sub>3</sub>

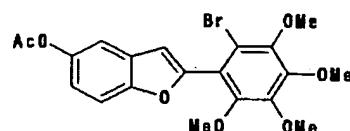
Ref. X1



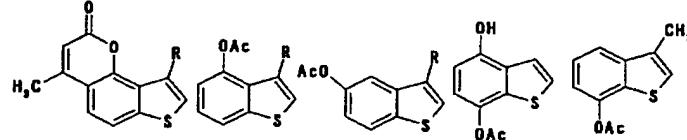
Ref. U2



Ref. V2

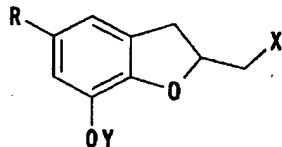


Ref. W2



R = H, Me

Ref. X2

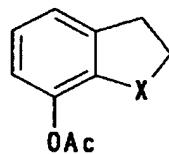


R = H, NO<sub>2</sub>;

X = Br, H-L-Cys(S)-OMe;

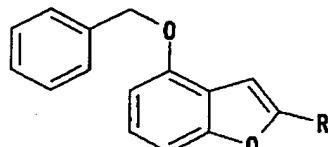
Y = CH<sub>3</sub>, Ac, Z-L-Ala

Ref. U3



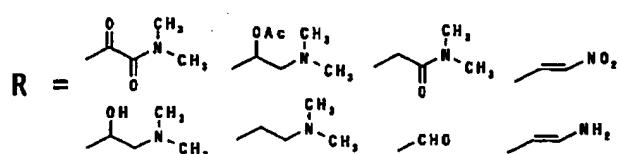
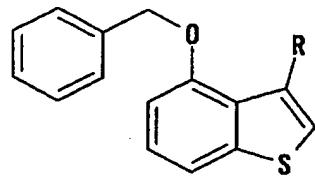
X = O, S

Ref. V3

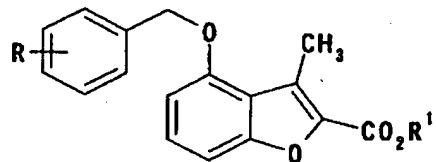


R = CO<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)(OH)CH<sub>3</sub>

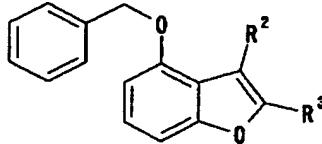
Ref. W3



Ref. X3



$R =$  4-Cl, 3-Cl, 3, 4-di-Cl,  
4-CO<sub>2</sub>H, 4-CN, 4-F, 4-CF<sub>3</sub>, 4-NO<sub>2</sub>,  
4-CH<sub>3</sub>O, 3-CH<sub>3</sub>O, 2-CH<sub>3</sub>O, 3, 4-di-CH<sub>3</sub>O,  
3, 5-di-Me, 3, 4-O(CH<sub>2</sub>)<sub>2</sub>O-, 3, 4-OCH<sub>2</sub>O-;  
 $R =$  CH<sub>3</sub>, H



$R^2 =$  CH<sub>3</sub>, (CH<sub>2</sub>)<sub>2</sub>Ph;  
 $R^3 =$  CONH<sub>2</sub>, C(=NH)OCH<sub>3</sub>, CN,  
2H-tetrazole, CH<sub>2</sub>CO<sub>2</sub>H, CO<sub>2</sub>H